

BP0309US-CP1

RECEIVED  
CENTRAL FAX CENTER  
DEC 12 2006

I. AMENDMENT**1. In the Specification**

In the sections of text to be amended, text deleted from the original appears in ~~strikethrough~~ and text to be added to the original has been underlined. The Examiner's attention is drawn to the fact that various numbers (that identify structures in the corresponding Figures) appearing in the original text were underlined and bold.

*Please delete the section of text at page 14, lines 1-12 and insert therefore the following text:*

With reference to Figure 3A and Example 8, the tert-butyldimethylsilyl (TBDMS) ester of (<sup>18</sup>O)<sub>2</sub> bromoacetic acid (14) was used in the alkylation reaction. This ester was prepared using <sup>18</sup>O labeled bromoacetic acid (13), obtained as a custom order from Cambridge Isotope Laboratory, Inc., and TBDMS-CN. The TBDMS ester of N-methyl piperazine acetic acid (15) was the product of the alkylation with N-methyl piperazine. The TBDMS ester was selected so that it could be converted to the acid chloride with, for example, oxalyl chloride thereby avoiding the requirement for any water and the possible exchange of <sup>18</sup>O with <sup>16</sup>O. In the presence of solid phase base (ss-TBD) and N-hydroxysuccinimide (NHS), the acid chloride was converted to the NHS ester (16). If the carboxylic acid is desired, instead of the active ester, the TBDMS ester could be converted to the carboxylic acid by treatment with an anhydrous acid such as TFA. Accordingly, aqueous treatment that might lead to <sup>18</sup>O ⇌ <sup>16</sup>O exchange, can be avoided whether to the active ester or the carboxylic acid is desired.

*Please delete the section of text at page 23, line 25 to page 24, line 2 and insert therefore the following text:*

The sample mixture can be prepared by mixing differing amounts of each sample. The sample mixture can be prepared by mixing equal amounts of each of the

BP0309US-CP1

samples. In this way there can be a direct comparison of the amount of each analyte (analyte by analyte) in each of the samples based upon the intensity of the peaks for the signature ions observed in the mass spectrometer. Whether or not equal amounts of sample are mixed together, the amount of each sample used to produce the sample mixture can be recorded. If unequal amounts of sample are used to prepare the sample mixture, appropriate ratios can be calculated from this information so that the relative and/or absolute amount (often expressed in concentration or quantity) of the analytes in the sample mixture can be determined based upon the intensity of the signature ion peaks.